

Appl. No. 09/646,111
Amendment dated: September 16, 2003
Reply to OA of: April 16, 2003

REMARKS

Applicants have amended the claims to more particularly define the invention taking into consideration the outstanding Official Action and to clarify the pending claims remaining in the application. In the Official Action the Examiner requests further clarification with regard to previously withdrawn or objected to claims. All of the claims have been canceled from the application without prejudice or disclaimer and new claims 42-52 have been added. Applicants most respectfully submit that all of the claims now present in the application are in full compliance with 35 U.S.C. 112 and are clearly patentable over the references of record.

Applicants appreciate the indication of allowable subject matter with respect to claims 20-24 in the Final Rejection of August 12, 2002. These claims have been canceled and replaced with claims 50-52 which are clearly allowable. However, see the corresponding subject matter of claims 39 -41 which has been rejected over the prior art. Claims 6, 11, and 14-17 were withdrawn from consideration as being directed to non-elected inventions, with no allowable generic claim in the application. It is submitted that claim 42 is an allowable generic claim and all of the remaining claims are either directly or indirectly dependent on claim 42 and are entitled to consideration on the merits.

Claim 42 is a combination of canceled claims 25, 28 and 29. Claims 43 and 44 correspond to canceled claims 26 and 27. Claim 45 corresponds to claim 30 and claim 46 to claims 31 and 32. Claim 47 corresponds to claim 34 and claims 48 and 49 to claims 37 and 38, respectively. Applicants most respectfully submit that all of the claims now present in the application are in full compliance with 35 USC 112 and are clearly patentable over the references of record.

Claim 39 has been objected to because of an informality in the misspelling of the word "ratio" in line 3. Applicants most respectfully request that this objection be withdrawn in view of the cancellation of claim 39.

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The rejection of claims 25-27, 29-31 and 33-38 under 35 U.S.C. 103(a) as being unpatentable over Hirao et al. U.S. 4,725,387, in view of Trofast et al., WO 95/0805 has been carefully considered but is most respectfully traversed in view of the amendments to the claims.

Claims 25-27, 29-31 and 33-38 have been canceled from the application and new claim 42 added which includes the limitation from canceled claim 28 not included in this rejection thereby obviating this rejection on this grounds alone. Applicants wish to clarify the issue of unpatentability over Hirao et al. in view of Trofast et al. with the following comments.

The Examiner is rejecting claim 25 on the basis of Hirao combined with Trofast and asserting that all features not found in this combination of documents namely, process steps b) and d) are of no criticality to the invention. Claims 28 and 32 are rejected to in light of all of the above plus Douglas. The Examiner's attention is also directed to MPEP section 2143.03 which states that all claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Applicants maintain the position that the rejected claims represent patentable subject matter and that the Examiner's rejections are merely based upon a hindsight mosaicing of two or three documents (along with conveniently ignoring all other features that cannot be found in these documents but which are claimed limitations). *In re Fritch*, 23 USPQ 1780, 1784(Fed Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.). However, in order to expedite the prosecution of this application, Applicants submit a further amended set of claims, new claims 42-52.

In the Official Action, it is urged that Hirao teaches a process of shaping crystals of sugar alcohols by obtaining a saccharified starch solution with high maltose content, allowing crystallization and separation. The Examiner notes that the viscosity of the

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solution can be regulated by addition of water-soluble organic solvent or elevated temperature. It is further noted that Hirao does not teach viscosity of less than 25 Pa.s at shear rate of 1s^{-1} , a claim limitation which cannot be ignored.

Applicants wish to point out that Hirao et al. is directed toward a very specific problem, i.e. a method for producing anhydrous crystals of maltitol. There is nothing in the teaching of this document to suggest to the skilled person that this methodology would be applicable to lactose or lactose monohydrate in accordance with the presently claimed invention.

It is also urged in the Official Action that Trofast teaches a stable crystallinic form of fine-grained substance or substance mixture useful for inhalation. The substance includes salbutamol sulfate, ipratropium bromide, or salmeterol xinafoate. Various carriers may be mixed with the substance and conditioned. Again, this combination of references does not suggest the presently claimed invention, absent Applicants' teaching which may not be used as a teaching reference. It is further stated that it would have been obvious for one of ordinary skill in the art to optimize the solid crystalline mixture of Hirao as a carrier useful for inhalation of pharmaceutical formulation in view of the teachings of Trofast. However, such a combination does not result in the presently claimed invention as it would result in a maltitol containing composition.

It is recognized in the Official Action that Hirao does not teach a viscosity of less than 25 Pa.s at a shear rate of 1s^{-1} . It is further urged that no criticality is seen in the particular viscosity since the prior art obtains the same result desired by Applicants, e.g. a crystalline composition that is non-hygroscopic, free-flowing and can be any desired size and shape. It is then concluded that it would have been *prima facie* obvious for one of ordinary skill in the art by routine experimentation to determine a suitable viscosity of the solution to obtain the claimed invention. These statements are specifically traversed.

Applicants most respectfully submit that the fact that a crystalline composition is obtained does not alter the fact that the obviousness of the claimed subject matter must

be considered in light of the claim limitations which include the viscosity range as set forth in the claims. There must be motivation in the prior art to make the necessary changes to the process and Applicants' specification may not be used as a teaching reference. Absent the suggestion in the prior art with respect to the viscosity range and steps specified in the rejected claims, there is no expectation of success and therefore the rejection should be withdrawn.

Douglas et al. does not teach the use of an aqueous solution of Carbomer as being a medium suitable for use in a crystallization process for lactose and lactose monohydrate in accordance with the presently claimed invention. The equivalence of starch and carbomers is not used in the same context as that of the present invention.

Applicants also most respectfully direct the Examiner's attention to MPEP § 2144.08 (page 2100-114) wherein it is stated that Office personnel should consider all rebuttal argument and evidence present by applicant and the citation of *In re Soni* for error in not considering evidence presented in the specification.

Applicants wish to note that crystals prepared according to the presently claimed invention have significantly higher mean elongation ratio and surface smoothness as discussed on page 10 of the present specification. See also page 11 of Applicants' specification. Moreover, data within this specification at page 28 demonstrates that increasing the surface smoothness and elongation ratio gives rise to an increase in the fine particle fraction (FFP) of the drug delivered. Hirao et al is silent as to these crystalline properties which are not suggested by the prior art. A skilled person would not be motivated to use in Hirao et al process in the expectation of producing crystals improved with these inhalation properties. Douglas et al. does not teach the use of an aqueous solution of carbomer as being a medium suitable for use in a crystallization process. The equivalence of starch and carbomers is not used in the same context as that of the present invention. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 28 and 32 under 35 U.S.C. 103(a) as being unpatentable over Hirao et al. in view of Trofast et al., and Douglas et al, has been carefully

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considered but in view of the above comments and further amendments to the claims. It is most respectfully requested that this rejection be withdrawn.

The rejection of claims 39-41 under 35 U.S.C. 103(a) as being unpatentable over Hirao et al., in view of Staniforth WO 96/23485 has been considered but is most respectfully traversed in view of the above comments. Hirao does not teach the process of making the lactose monohydrate in accordance with the present invention and does not contain the necessary motivation to lead one of ordinary skill in the art to the lactose monohydrate within the size limitation and elongation as claimed. Note also the properties associated with the claimed subject matter as set forth in the working examples in Applicants' specification. It is therefore, most respectfully requested that this rejection be withdrawn.

In view of the above comments and further amendments to the claims, favorable reconsideration and allowance of all of the claims now present in the application are most respectfully requested.

Respectfully submitted,

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